

Notice of Allowability

Application No.

09/094,921

Examiner

Anne Holleran

Applicant(s)

LINDHOFER ET AL.

Art Unit

1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to amendment filed 6/27/2005.
2. ☒ The allowed claim(s) is/are 1-8, 13-21, 23, 26 and 32-34.
3. ☐ The drawings filed on _____ are accepted by the Examiner.
4. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☒ All b) ☐ Some* c) ☐ None of the:
 1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 6. ☒ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☒ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☒ to Paper No./Mail Date 5/24/2000.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date 20050801.
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

Alana M. Harris
ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER
08/08/2005

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Chuan Gao on 8/3/2005.

The application has been amended as follows:

In the specification:

At page 12, line 14, the phrase "described for instance in claim 9" was replaced by the following: "having isotype combinations of the above described heterologous intact bispecific antibodies".

In the claims:

In claim 1, line 1, the word "Method" was substituted by the phrase "A method".

Claim 2. The Method method according to claim 1, in which said antibodies ~~are selected so that they are capable of binding~~ bind Fc receptor-positive cells having a Fc γ receptor I, II, or III.

In claim 3, line 1, the word "Method" was substituted by the phrase "The method".

Claim 4. The Method method according to claim 1, in which said antibodies ~~are~~ capable of inducing induce tumor-reactive complement-binding antibodies, thereby and thus inducing a humoral immune response.

Claim 5. The Method method according to claim 1, in which said antibodies ~~are~~ selected to bind to the T cells via CD2, CD3, CD4, CD5, CD6, CD8, CD28 or CD44.

Claim 6. The Method method according to claim 1, in which said antibodies, ~~are~~ selected so that following their binding to the Fc receptor-positive cells, initiate or increase the expression of co-stimulatory antigens CD40, CD80, CD86, ICAM-1 and /or LFA-3 ~~as co-stimulatory antigens~~, and/or initiate or increase the secretion of cytokines by the Fc receptor-positive ~~cell is initiated or increased~~ cells.

Claim 7. The Method method according to claim 1, in which said antibodies ~~are~~ selected so that increase the secretion of IL-1, IL-2, IL-4, IL-6, IL-8, IL-12 ~~being cytokines or of~~ TNF- α or a combination thereof ~~is increased~~.

Claim 8. The Method method according to claim 1, in which said bispecific antibody is ~~selected to be an anti-CD3 X anti-tumor-associated antigen antibody or anti-CD4 X anti-tumor-associated antigen antibody or anti-CD5 X anti-tumor-associated antigen antibody or anti-CD6 X anti-tumor-associated antigen antibody or anti-CD8 X anti-tumor-associated antigen~~

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antibody or anti-CD2 X anti-tumor-associated antigen antibody or anti-CD28 X anti-tumor-associated antigen antibody or anti-CD44 X anti-tumor-associated antigen antibody.

Claim 14. A method for preparing a vaccine comprising activated peripheral blood mononucleated cells, said method comprising preparing an antibody-tumor cell preparation by a method comprising steps (a) and (b) of the method of claim 1 in which step (e) is replaced with step (d), which comprises and further comprising the step of incubating the thus-treated tumor cells with both intact heterologous bispecific antibodies and peripheral blood mononucleated cells, thereby activating said peripheral blood mononucleated cells, and preparing a vaccine from the thus-activated peripheral blood mononucleated cells, wherein said intact heterologous bispecific antibodies have the following properties:

- (i) binding to a T cell;
- (ii) binding to at least one tumor-associated antigen on a tumor cell;
- (iii) binding by their Fc portion to Fc receptor-positive cells; and
- (iv) capable of activating the Fc receptor-positive cell whereby the expression of cytokines, co-stimulatory antigens or both is induced or increased,

and said bispecific antibodies have isotype combinations selected from the group consisting of:

- rat-IgG2b/human-IgG1,
- rat-IgG2b/human-IgG2,
- rat-IgG2b/human-IgG3[oriental allotype G3m(st) = binding to protein A],
- rat-IgG2b/human-IgG4,

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rat-IgG2b/rat-IgG2c,
mouse-IgG2a/human-IgG3 [caucasian allotypes G3m(b+g) = no binding to
protein A, in the following indicated as *],
mouse-IgG2a/mouse-[VH-CH1, VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],
mouse-IgG2a/rat-[VH-CH1, VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],
mouse-IgG2a/human-[VH-CH1, VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],
mouse-[VH-CH1, VL-CL]-human-IgG1/rat-[VH-CH1, VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],
mouse-[VH-CH1, VL-CL]-human-IgG4/rat-[VH-CH1, VL-CL]-human-IgG4-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2: > aa position 251]-human-IgG3*[CH3],
rat-IgG2b/mouse-[VH-CH1, VL-CL]-human-IgG1-[hinge-CH2-CH3],
rat-IgG2b/mouse-[VH-CH1, VL-CL]-human-IgG2-[hinge-CH2-CH3],
rat-IgG2b/mouse-[VH-CH1, VL-CL]-human-IgG3-[hinge-CH2-CH3, oriental allotype],
rat-IgG2b/mouse-[VH-CH1, VL-CL]-human-IgG4-[hinge-CH2-CH3],
human-IgG1/human-[VH-CH1, VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

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human-IgG1/rat-[VH-CH1, VL-CL]-human-IgG1-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

human-IgG1/mouse-[VH-CH1, VL-CL]-human-IgG1-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

human-IgG1/rat-[VH-CH1, VL-CL]-human-IgG1-[hinge]-human-IgG2[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

human-IgG1/mouse-[VH-CH1, VL-CL]-human-IgG1-[hinge]-human-IgG2[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

human-IgG1/rat-[VH-CH1, VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

human-IgG1/mouse-[VH-CH1, VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

human-IgG2/human-[VH-CH1, VL-CL]-human-IgG2-[hinge]-human-IgG3*-[CH2-CH3],

human-IgG4/human-[VH-CH1, VL-CL]-human-IgG4-[hinge]-human-IgG3*-[CH2-CH3],

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human-IgG4/human-[VH-CH1, VL-CL]-human-IgG4-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

mouse-IgG2b/rat-[VH-CH1, VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-IgG2b/human-[VH-CH1, VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-IgG2b/mouse-[VH-CH1, VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-[VH-CH1, VL-CL]-human-IgG4/rat-[VH-CH1, VL-CL]-human-IgG4-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

human-IgG1/rat-[VH-CH1, VL-CL]-human-IgG1-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

human-IgG1/mouse-[VH-CH1, VL-CL]-human-IgG1-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

human-IgG4/human-[VH-CH1, VL-CL]-human-IgG4-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

rat-IgG2b/mouse-IgG2a,

rat-IgG2b/mouse-IgG2b, and

rat-IgG2b/mouse-IgG3.

In claim 15, line 1, the word "Method" was substituted by the phrase "The method".

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In claim 16, line 1, the word "Method" was substituted by the phrase "The method".

In claim 17, line 1, the word "Method" was substituted by the phrase "The method".

In claim 18, line 1, the word "Method" was substituted by the phrase "The method".

In claim 19, line 1, the word "Method" was substituted by the phrase "The method".

In claim 20, line 1, the word "Method" was substituted by the phrase "The method".

In claim 21, line 1, the word "Method" was substituted by the phrase "The method".

In claim 23, line 1, the word "Method" was substituted by the phrase "A method".

REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance: The amendment obviated the rejection of the claims under 112, 2nd paragraph, and the rejections of claims 31 and 35 (canceled by amendment) under 35 U.S.C. 102(b) over Honsik and also over Renner.

The provisional obviousness-type double-patenting rejection of claims 1-8, 13-21, 23 and 26 as being unpatentable over claims 1,7,10,19,22 and 23 of copending Application No. 10/378,218 is withdrawn because according to MPEP 822.01, if a provisional double patenting rejection is the only remaining rejection in the case following entry of an amendment, the examiner should withdraw the rejection and permit the application to issue as a patent. In this case, the amendment filed 6/27/2005 obviated all of the other rejections of record, and the only remaining rejection was the provisional double patenting rejection. Therefore, the double patenting rejection is withdrawn.

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Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (571) 272-0833. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 5:30 pm.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 571-1600.

Anne L. Holleran

Patent Examiner

August 3, 2005


ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER